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MECHANISMS THAT DEFEND THE BODY FROM POLIOMYELITIC  
INFECTION, (a) EXTERNAL OR EXTRA-NERVOUS,  
(b) INTERNAL OR NERVOUS

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I am led to report the results of recent experiments looking toward the solution of the problem of susceptibility in epidemic poliomyelitis, by reason of the intrinsic interest of the subject and because of certain advances in knowledge which have been made recently.

The mass of the population appears insusceptible to the disease. That is to say even under conditions in which poliomyelitis is severely epidemic the real incidence is low. Thus the incidence during the past summer and autumn in Greater New York City, in which more than 9000 cases of the disease were recognized, was 1.59 per 1000 of the population.

Our present knowledge indicates that during epidemics, the microbic cause or virus of the disease is very widespread. This virus leaves and enters the body by way of the nasal and buccal mucous membranes. It is present not only in paralyzed persons but equally in the greater number of the affected who are often only slightly ill and do not develop any paralysis whatever, and in an undetermined number of healthy persons who have been in intimate contact with both classes of patients mentioned.

In view of the wide distribution of the virus and the relatively low case incidence, we must suppose that many more persons are exposed to than acquire the infection. Hence the body must possess defensive mechanisms usually sufficing to protect it from invasion.

Two sets of defences have been detected. The first or external consists of the secretions of the nasal and probably pharyngeal mucous membranes. Their action has been especially studied by Amoss and Taylor.<sup>1</sup> The secretions in many if not in most persons when left in contact for a relatively short time with the virus of poliomyelitis, inactivate or neutralize it. This test is readily made because monkeys are highly susceptible to inoculation with the virus. When an active virus has been mixed with the bacteria-free nasal secretions obtained by filtration through porcelain, it is no longer active for monkeys.

Some persons fail to yield this neutralizing nasal secretion; in others, a temporary, pathological state of the mucous membranes removes the inactivating property previously present. The number of tests is still

too small to determine whether young persons who are the more susceptible yield secretions which are numerically inferior in neutralizing power to those supplied by older persons.

Probably the failure of this external defensive measure is not in itself decisive, because of the existence of the second or inner defensive mechanism. It consists of the membranes about the brain and spinal cord and attached secreting organ of the choroid plexus. This meningeal-choroid complex is remarkably efficient in excluding from the cerebrospinal fluid, and hence from the substance of the brain and spinal cord, almost everything present in the circulating blood, except water and a few inorganic salts. The fluid is also almost free of cells. Only when the complex has been injured in some way and its integrity impaired does it permit even protein and cells to pass through from the blood into the cerebrospinal fluid.

The fact had previously been determined,<sup>2</sup> that the virus of poliomyelitis passes with great difficulty from the blood into the nervous organs, unless the choroid plexus and meninges had previously been injured, say through setting up an aseptic inflammation by injecting sterile horse serum into the meninges by means of lumbar puncture. What the present studies have brought out is the extraordinary sensitiveness of those structures to the injurious action of otherwise bland fluids,<sup>3</sup> for not only is their permeability affected by irritants such as horse and even normal monkey serum, both of which produce visible signs of inflammation, but also by sterile physiological salt, Ringer's or Locke's solutions which set up only evanescent inflammatory changes, and of the cerebrospinal fluids from other monkeys which produce no detectable inflammatory changes whatever. The injury produced by the last fluid mentioned is so slight as possibly to be regarded in Cohnheim's sense as merely molecular.

Possibly poliomyelitis arises during the prevalence of the malady when both sets of defensive measures fail. This probably would occur only in exceptional instances in individuals among populations of any size. It is for the moment not difficult to conceive of reasons to account for the failure of the external mechanism, and more difficult to account for failure of the internal mechanism of defense. Not improbably the neutralizing power of the nasal secretions tends to reduce the carriage of the virus upon the nasal mucosa of persons exposed to and having suffered from infection with the virus of poliomyelitis. It becomes, therefore, an essential agency in diminishing public danger through reduction in the number of the potential virus carriers which arise.

There is one irritating fluid only so far detected which does not pro-

mote infection when injected into the cerebrospinal meninges. This fluid is an immune serum obtained from monkeys or human beings previously recovered from poliomyelitis. The immune serum carries neutralizing principles which inactivate the virus as it passes from the blood into the cerebrospinal fluid. This observation is in harmony with the curative action exercised by the serum, as was first shown some years ago in inoculated monkeys,<sup>4</sup> and has recently been confirmed for human cases of epidemic poliomyelitis.<sup>5</sup>

<sup>1</sup> Amoss, H. L., and Taylor, E., *J. Exp. Med.*, **25**, 1917, (507).

<sup>2</sup> Flexner, S., and Amoss, H. L., *Ibid.*, **19**, 1914, (411).

<sup>3</sup> Flexner, S., and Amoss, H. L., *Ibid.*, **25**, 1917, (525).

<sup>4</sup> Flexner, S., and Lewis, P. A., *J. Amer. Med. Assn.*, **54**, 1910, (1780); **55**, 1910, (662).

<sup>5</sup> Amoss, H. L., and Chesney, A. M., *J. Exp. Med.*, **25**, 1917, (581).

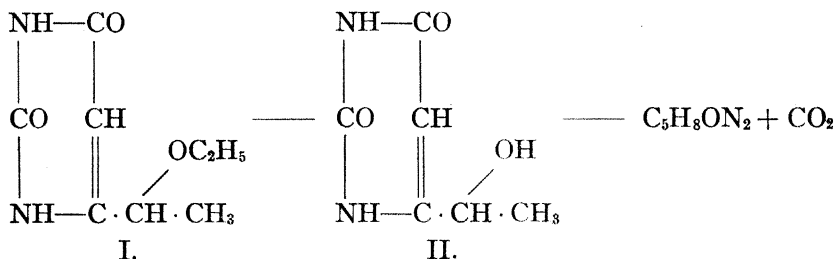
## THE BEHAVIOR ON HYDROLYSIS OF THE SIMPLEST SECONDARY NUCLEOSIDE ON THYMINE

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Communicated by L. B. Mendel, May 5, 1917

In a previous publication from the Sheffield Chemical Laboratory Johnson and Hadley<sup>1</sup> have shown that the ethyl ether of the secondary uracil-nucleoside I undergoes a very unique transformation when subjected to hydrolysis by heating with hydrobromic acid in aqueous solution. Ethyl bromide is first evolved with formation of the nucleoside II. This pyrimidine then undergoes a profound molecular change on prolonged heating and is transformed, with evolution of carbon dioxide, into a combination of unknown structure having the empirical formula  $C_5H_8ON_2$ .



Great biochemical interest is attached to nucleoside transformations of this character, and we have now in progress an investigation planned to establish experimentally the structure of this interesting product of hydrolysis.